Ref. 8

MARCH 10, 1956

6 29 MAR 1956
Con Copy

PAGES 317 TO 324

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2
Telegrams: LANCET, RAND, LONDON Telephone: TEMPLE BAR 7228 and 7229

No. X OF VOL. I, 1956
No. 6915 VOL. CCLXX

LONDON, SATURDAY, MARCH 10, 1956
Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper

Pp. 8—Price 1s. 6d.
Annual Subscription: £3 3s.

Hypofibrinogenæmia in Pregnancy

SERIOUS loss of blood from the uterus after labour is one of the major complications of childbirth and one of the commonest causes of death of the mother. The collection of incidents and information over the past ten years has led obstetricians to recognise that the immediate cause of the disastrous uterine hæmorrhage is often a temporary abnormality of the blood-clotting process; and furthermore, if treated in time, these hæmorrhages can be stopped and the patient saved by other than local methods. RATNOFF et al.[1] have recently reviewed the evidence and come to the conclusion that abnormal blood-clotting is the usual cause of fatal uterine post-partum hæmorrhage.

In normal pregnancy and labour blood-clotting processes are little changed. There are no significant changes in the platelet-count and no unusual fibrinolytic activity in the plasma. The fibrinogen content of the plasma rises slowly by about one-third during the pregnancy. After labour it is, as BARNES [2] pointed out, the contraction of the myometrium that ensures proper hæmostasis at the placental site; the most striking examples of this have been seen in patients with thrombocytopenic purpura [3] and in a young woman with hæmophilia [4] who have successfully completed labour without any unusual *immediate* blood-loss; subsequent blood-loss in these patients came from damage to other parts of the genital tract that are not supplied with such an efficient vasoconstrictor apparatus as the uterus. The obstetric conditions especially liable to be followed by excessive uterine hæmorrhage are premature separation of the placenta, amniotic-fluid embolism, missed abortion with retention of a dead fœtus, and eclampsia. It has been discovered that, except in eclampsia, the blood-clotting abnormality in all these conditions is a gross deficiency of fibrinogen, and the explanation proposed is that thromboplastic material reaches the maternal circulation. Experimental evidence for this hypothesis has been known for some time. RATNOFF et al.[1] quote experiments by MILLS in 1921 which showed that intravenous injection of tissue-thromboplastin caused a decrease of plasma-fibrinogen, and in fact gradual infusion of thromboplastin led to complete defibrination of the animal; the fibrinogen level in the plasma returned to normal twenty-four hours after the infusion ceased. There is also evidence that amniotic fluid and placental tissue have considerable thromboplastic activity. Hæmorrhagic symptoms appear when the plasma-fibrinogen level falls below 100 mg. per 100 ml.: there is often bleeding from venepuncture sites and subcutaneous hæmorrhage; and postpartum uterine bleeding may be severe and prolonged and the consequences grave.

Premature separation of the placenta is the commonest cause of uterine bleeding in pregnancy and is said to occur in from 1 in 85 to 1 in 250 pregnancies. The condition has been known for twenty years to be associated with hypofibrinogenæmia, but only lately has this point received much attention. The cause is thought to be the passage of thromboplastic material from the placenta into the maternal blood-vessels, where intravascular clotting takes place, and this continuing process uses up the plasma-fibrinogen; but this explanation is not accepted by all authorities. In amniotic-fluid embolism, the sudden onset of labour and its rapid course is sometimes followed by severe uterine hæmorrhage, and hypofibrinogenæmia is often found; JACKSON et al.[5] have recorded 8 such cases. The latest syndrome to be associated with plasma-fibrinogen depletion is missed abortion with retention of a dead fœtus in the uterus. WEINER et al.[6] described 3 cases of severe uterine hæmorrhage following spontaneous delivery of a dead fœtus, in which hypofibrinogenæmia was found in the mother; they thought that rhesus incompatibility was also concerned, but subsequent findings do not support this view. PRITCHARD and RATNOFF [7] studied 31 patients who remained undelivered for three or more weeks after apparent intra-uterine fœtal death: in 23 there was no evidence of critical depletion of fibrinogen (i.e., a level below 150 mg. per 100 ml.), though in 7 patients the fibrinogen level fell steadily throughout the pregnancy; in the remaining 8 patients the fibrinogen levels became dangerously low. After delivery the plasma-fibrinogen rose rapidly to normal in forty-eight hours. Experience has shown that hypofibrinogenæmia does not develop when the fœtus dies before the fourth month of gestation, and it does not appear until at least five weeks after the apparent death of the fœtus.

Lately cases of hypofibrinogenæmia in pregnancy have been reported in this country. BARNETT and CUSSEN [8] described 2 cases of concealed accidental hæmorrhage causing precipitate labour; qualitative tests showed a low fibrinogen level. BARRY et al.[9] gave details of 6 cases of complications of pregnancy associated with hypofibrinogenæmia; and in 1 of them none of the recognised syndrome was present. KELSEY and MUIRHEAD [10] also described fibrinogen deficiency in an apparently uncomplicated case of postpartum hæmorrhage. O'DRISCOLL and LAVELLE [11] had a patient with a retained dead fœtus and low plasma-fibrinogen, low platelet-count, and an active fibrinolysin in the plasma. When induction by an oxytocin drip failed, a hysterectomy was carried out; and it is interesting that no large retroplacental hæmatoma was found, because such a hæmatoma has been suggested as the source of the thromboplastin which reduces the plasma-fibrinogen. KIMBELL and GHOSH [12] found afibrinogenæmia associated with massive postpartum hæmorrhage after a lower-segment cæsarean section.

In the matter of treatment, RATNOFF and his colleagues agree with MOLONEY et al.[13] that human fibrinogen

1. Ratnoff, O. D., Pritchard, J. A. Colopy, J. E. *New Engl. J. Med.* 1955, **253**, 63, 97.
2. Barnes, A. C. *Amer. J. med. Sci.* 1947, **213**, 463.
3. Epstein, R. D., Lozner, E. L., Cobbey, T. S., Davidson, C. D. *Amer. J. Med.* 1950, **9**, 44.
4. Israels, M. C. G., Lempert, H., Gilbertson, E. *Lancet*, 1951, **1**, 1375.
5. Jackson, D. P., Hartmann, R. C., Busby, T. *Obstet. Gynec.* 1955, **5**, 223.
6. Weiner, A. E., Reid, D. E., Roby, C. C., Diamond, L. K. *Amer. J. Obstet. Gynec.* 1950, **60**, 1015.
7. Pritchard, J. A., Ratnoff, O. D. *Surg. Gynec. Obstet.* 1955, **101**, 467.
8. Barnett, V. H., Cussen, C. A. *Brit. med. J.* 1954, **ii**, 676.
9. Barry, A. P., Geoghegan, F., Shea, S. M. *Ibid.* 1955, **ii**, 287.
10. Kelsey, H. A., Muirhead, J. M. B. *Lancet*, 1955, **ii**, 705.
11. O'Driscol, D. T., Lavelle, S. M. *Ibid.*, p. 1169.
12. Kimbell, N., Ghosh, A. K. *Ibid*, Jan. 14, 1956, p. 82.
13. Moloney, W. C., Egan, W. J., Gorman, A. J. *New Engl. J. Med.* 1949, **240**, 596.

should be given intravenously as soon as possible; the initial dose should be 4 g., and this may be enough or may need to be repeated later. If fibrinogen is not available, blood can be given, taking 1 litre of blood to correspond to 1·5 g. of fibrinogen. The American workers agree that in all these patients the uterus should be emptied as soon as possible if labour does not ensue within twelve hours of induction, since the fibrinogen level always rises within forty-eight hours of delivery. If treatment is to be effective, it must be given promptly; so some method for the quick assessment of the fibrinogen level in the plasma is needed. BARRY et al.[6] give details of a method for a rapid but rough assay based on an original method of SCHNEIDER, and also of a rapid biuret method, devised by SHEA, which gives a rough quantitative answer in ten minutes and a 90% accurate estimation in thirty minutes. PRITCHARD and RATNOFF[7] describe a very simple "clot observation test"; blood carefully withdrawn from a vein is run into a small tube containing a little bovine thrombin (now commercially available). Normally a firm clot should form in a few seconds; in hypofibrinogenæmia a clot may form, but it soon retracts, spontaneously or on tapping the tube, into a small ball from which most of the red cells are extruded. Once the diagnosis of hypofibrinogenæmia is established, emptying of the uterus should be carefully considered, though the case-records suggest that dangerous hæmorrhage is not inevitable. If bleeding has to be dealt with, the best treatment is certainly the intravenous injection of fibrinogen as soon as possible. As most of the National Blood Transfusion Centres in this country hold stocks of dried human fibrinogen available for immediate use, treatment need not be long delayed. The prognosis is usually good, but sometimes, especially with amniotic-fluid embolism, the patient dies despite the administration of fibrinogen. Awareness of the possible diagnosis and prompt treatment can, it is clear, eliminate almost completely this cause of maternal mortality.

Impetigo

IN the past, impetigo has been attributed to infection with either *Staphylococcus aureus*, *Streptococcus pyogenes*, neither, or both. HOPE SIMPSON,[1] in 1941, argued that impetigo was a specific infection which "bred true": it was not contracted from patients with boils, nor did it give rise in contacts to pyogenic lesions of other kinds. Such a specific superficial reaction of the skin must therefore be due to an organism with peculiar properties and for this he proposed the name "impetigococcus." The specificity of the responsible organism was also suggested by SPITTLEHOUSE,[2] who reported a small series in which he had carried out phage-typing of staphylococci derived from impetigo and sycosis barbæ. In the former he found 81% of phage-type 71, but only 14% were of this type in the sycosis group. Moreover, the majority of impetigo organisms were penicillin-resistant.

These findings have been abundantly confirmed in two larger studies. BARROW[3] found type-71 staphylococci in 80% of strains recovered from impetigo, contrasting with about 6% of this type in strains derived from a large control group. Penicillin resistance in vitro was demonstrated in 71% of staphylococci from impetigo, and of the resistant organisms 84% were type 71. The results of PARKER et al.[4] are closely similar. Of *Staph. aureus* strains derived from impetigo, three-quarters were of type 71 and most of them were penicillin-resistant.

It seems unlikely that the high incidence of type-71 staphylococci in all three reports is due to a purely local distribution of the organism; for the areas concerned are reasonably far apart—Sheffield, Bradford, and Manchester. PARKER et al. also examined cultures from impetigo lesions supplied by various Public Health Laboratories in widely separated areas and found that type-71 staphylococci were common in all. The suspicion naturally arose that since many of the organisms were penicillin-resistant, they might have been hospital bred under the penicillin parasol. This seems to be disproved, however, by the fact that most penicillin-resistant staphylococci are of phage-types other than type 71. (In fact type-71 organisms were rarely recovered by PARKER and his colleagues from superficial skin infections other than impetigo and they were absent in deep infections such as boils.) Moreover, PARKER et al. also report an investigation carried out in Cambridge in 1941 before phage-typing was adopted. In this study, it was found that staphylococci derived from impetigo in young Servicemen had the property of inhibiting the growth of corynebacteria in 47% of cases. (This property was present in only 19% of staphylococci derived from other skin lesions and in 10% of those from nose and throat swabs.) Repeating these studies in the recent investigation they found that 90% of type-71 staphylococci *and very few others* had this property of inhibition. This led to the tantalising supposition that the organisms studied in 1941 before penicillin came into use were probably also penicillin-resistant.

BARROW doubts whether the presence of staphylococci in the nose is of the same significance in impetigo as it appears to be in deeper pyogenic infections (VALENTINE and HALL-SMITH,[5] for example, reported up to 80% nasal carriage in furunculosis and as high as 91% in sycosis barbæ). In BARROW's series, 46% of cases of impetigo carried the same staphylococcal type in the nose and in the skin lesions, but in his control groups a similar rate of nasal carriage of staphylococci was discovered. He feels that if nasal carriage were important in the origin of impetigo, the rate would be much higher. Moreover, his cases of impetigo did not recur or relapse although no nasal treatment was given.

These recent papers also consider the rôle of streptococci in impetigo. BARROW cultured *Staph. aureus* alone in 81% of lesions, *Strep. pyogenes* alone in 5·6%, and a mixed growth in 13·2%. He considers that in a third of the patients yielding the streptococcus it was probably the primary cause and that it was a secondary invader in the remainder. PARKER et al. report that of the streptococci recovered from their patients, three-quarters were of one of two closely related serological types, one of which was rarely found in other situations.

These findings therefore support the conclusion that impetigo is a fairly distinct infection and that it is not an opportunist invasion by arbitrary organisms which happen to reside normally on the skin. BARROW says that "there seems to be good clinical, epidemiological and bacteriological evidence in favour of the existence of two forms of impetigo, caused by staphylococci and streptococci respectively." It is interesting to note, however, that "no clinical distinction was observed between those lesions yielding pure staphylococci and those yielding pure streptococci," and it is clear that, as PARKER and his colleagues say, there is further need for correlation of clinical and bacteriological findings in this disease.

Patent Ductus Arteriosus

THE diagnosis of patent ductus arteriosus is seldom difficult in a typical case with a continuous machinery murmur in the pulmonary area. With shunts of any size from aorta to pulmonary artery, there will be in addition a collapsing pulse, distension and pulsation of the pulmonary artery and its branches, and perhaps left ventricu-

1. Hope Simpson, R. E. *Lancet*, 1941, i, 683.
2. Spittlehouse, K. E. *Ibid*, 1955, ii, 378.
3. Barrow, G. I. *J. Hyg., Camb.* 1955, **53**, 495.
4. Parker, M. T., Tomlinson, A. J. H., Williams, R. E. O. *Ibid*, p. 458.
5. Valentine, F. C. O., Hall-Smith, S. P. *Lancet*, 1952, ii, 351.

lar hypertrophy. An apical diastolic murmur which sometimes confuses the diagnosis, and which may indeed be due to coincidental abnormalities of the mitral valve, usually indicates a large shunt with an excessive blood-flow through the left heart. The shunt is usually small; but in the more severe cases, with pulse-pressures between 60 and 100 mm. Hg, it may amount to 50–70% of the left ventricular output. There is general agreement that surgical closure of a patent ductus is almost always advisable both because of the risk of bacterial endocarditis and because of the natural history of the disease. Admittedly, large shunts can be tolerated for a surprisingly long time, and spontaneous closure is possible even after the age of thirty; but deterioration with heart-failure is to be expected, as CAMPBELL has found, in the third or fourth decade.[1]

An important and peculiar complication of patent ductus arteriosus is pulmonary hypertension.[2-5] It is perhaps less common with patent ductus arteriosus than with other congenital communications such as atrial or ventricular septal defects[6]; but there is evidence to suggest that at least 1 case in 10 may be affected. Two forms can be recognised: one which develops gradually and is usually mild, and the other which begins early and is severe. Its effect is to reduce or abolish the shunt or even reverse its usual direction; and the clinical signs are modified accordingly. In the mild form the continuous murmur may persist, although it is usually shortened to a systolic murmur, and it often disappears altogether in the severe form. The pulse-pressure tends to remain large, but symptoms and signs of pulmonary hypertension develop and may even predominate. Attacks of respiratory infection, with cough, dyspnœa, and hæmoptysis, are common, and ultimately there is right-sided heart-failure. The pulmonary second sound is loud and accentuated, and it is accompanied by a palpable impulse in the second left intercostal space. The characteristic parasternal lift of a hypertrophied right ventricle can usually be found; and the electrocardiogram often indicates right ventricular or combined right and left ventricular strain. Giant *a* waves can sometimes be seen in the jugular pulse, and a Graham Steel diastolic murmur of pulmonary incompetence may suggest a diagnosis of aortic incompetence unless the significance of the other signs is appreciated. Reversal of the shunt usually causes cyanosis, which can be generalised but is often more pronounced in the lower limbs because of the entry of the ductus into the aorta beyond the left subclavian artery.

Recognition of a patent ductus arteriosus combined with pulmonary hypertension can be difficult. Where the continuous murmur persists the diagnosis should be possible clinically, but when the signs of pulmonary hypertension predominate, the diagnosis from other lesions, such as atrial and ventricular septal defects and primary pulmonary hypertension, can be made only after catheterisation and angiocardiography.[7] Indeed the possibility of an underlying patent ductus arteriosus makes such investigations essential in any patient with unexplained pulmonary hypertension, whether cyanosed or not, particularly in children. Catheterisation by itself will sometimes be enough, for the catheter often passes easily through the ductus, especially if the shunt is reversed. In uncyanosed cases there should be a higher oxygen saturation in the pulmonary artery than in the right ventricle; and an angiocardiogram may show simultaneous filling of the pulmonary artery and the descending aorta.

The cause of pulmonary hypertension in patent ductus arteriosus is debatable. Mild hypertension coming on in middle life may be due to an increase in pulmonary blood-flow; but this can hardly account for severe hypertension, since shunts amounting to 50% of the left ventricular outflow often persist uncomplicated for a number of years. Pulmonary resistance is always increased when the shunt is reversed, and this increase is almost certainly what produces severe pulmonary hypertension. Why resistance should increase is not clear: histological studies have suggested that repeated pulmonary embolism and even acute pulmonary arteriolitis are occasionally responsible, but persistence of a fœtal pattern of thick-walled and muscular arteries has been suggested by EDWARDS[8,9] as a more likely explanation. On the other hand, widespread arterial occlusion by fibrous tissue, associated with the formation of new and probably anastomotic vessels, as recently described by BREWER[10], suggests that the vascular abnormality is sometimes acquired as the late result of an earlier functional change.

Opinion varies about the treatment of patent ductus arteriosus with hypertension. The need for operation is clearly increased by slight hypertension, but it is debatable in the severer grades. Where there is cyanosis indicating a reversed shunt, operation is contra-indicated, since the ductus seems to act as a safety valve. Some people advocate ligation in all cases with left-to-right shunt, claiming that its effects are beneficial even some time afterwards. Others prefer to be guided by the effects on the pulmonary pressure of digital compression of the ductus at the time of operation, since success depends upon the reversibility of the hypertension. The technical difficulties may be formidable because the ductus is often short and wide and may contain calcium, which can spread on to the pulmonary artery or the aorta and make them liable to tear.

1. Campbell, M. *Brit. Heart J.* 1955, **17**, 511.
2. Cosh, J. A. *Ibid*, 1953, **15**, 423.
3. Damman, J. F., Sell, C. G. R. *Circulation*, 1952, **6**, 110.
4. Johnson, R. E., Werner, P., Kerschner, M., Cournand, A. *Ibid*, 1950, **1**, 1293.
5. Wood, P. St. Cyres Lecture, 1951.
6. Shephard, R. J. *Brit. Heart J.* 1954, **16**, 361.
7. Whitaker, W., Heath, D., Brown, J. W. *Ibid*, 1955, **17**, 121.
8. Edwards, E. *Amer. Heart J.* 1948, **28**, 206.
9. Hullgren, H., Selzer, A., Purdy, A., Holman, E., Gerbode, F. *Circulation*, 1953, **8**, 15.
10. Brewer, D. B. *J. Path. Bact.* 1955, **70**, 999.

Annotations

BRITISH POLIOMYELITIS VACCINES

THE department of biological standards of the National Institute for Medical Research is responsible for carrying out the safety tests on the poliomyelitis vaccines soon to be used in this country, and the director of the department, Dr. W. L. M. Perry, has sent us some detailed technical information about the vaccines. In our present difficulties it is impossible to publish this information in full, but Dr. Perry's text will be found in this week's *British Medical Journal*. The most important modification from the strains of virus used in the United States is the adoption of an alternative type-1 virus which is considerably less virulent than the original strain, a change which should greatly increase the safety of the vaccines. The method of vaccine production and formalin treatment are similar to those used elsewhere, and the British vaccines will be subjected in duplicate to all the safety tests adopted in the U.S.A., including the use of cortisone-treated monkeys. As Dr. Goffe emphasised in our last issue, the American vaccine which has met these new requirements has been given to some 10 million children without any detectable ill-effects. It is hoped that British vaccines will be at least as potent as American vaccines and Dr. Perry calls for the support of the medical profession in this first step towards the safe and effective control of poliomyelitis in this country.

In the past few days general practitioners received from the Ministry of Health a note giving information about poliomyelitis vaccination. The Medical Research Council has been invited by the Ministry to assess the efficacy of the British vaccines; and medical officers of health will be asked to make a brief report on each notified case, paralytic or non-paralytic, in their areas in children born in 1947-54.

DECORTICATION IN PULMONARY TUBERCULOSIS

DECORTICATION of the lung has proved less successful in pulmonary tuberculosis than in traumatic hæmothorax. In tuberculosis involvement of the underlying lung gives rise to difficulty in removing the "peel," and thus to subsequent air-leaks which may prevent expansion of the lung; failure may also result from hæmorrhage or infection.[1] Yet as experience grows, the results are becoming more encouraging. Thus Savage and Fleming[2] report from Sully Hospital that the majority of their tuberculous patients who underwent decortication of the lung showed significant functional improvement. In each of 34 cases where a persistent pleural space, infected or uninfected, was present, this was obliterated without inducing mediastinal shift; indeed where mediastinal shift was present preoperatively, it was at least partly reduced by the operation. In only 2 instances was thoracoplasty required to aid obliteration; but in 3 other instances thoracoplasty was carried out to control disease in the lung after the space had been obliterated by decortication. One woman, aged 47, in whom thickened pleura had been present for twenty years, and who had shortness of breath on the slightest exertion and severe œdema of the ankles, was able to continue her life as a school-teacher with much-improved exercise tolerance as a result of freeing her constricted left lung and restoring her displaced mediastinum to a more central position.

Such spectacular results are exceptional. Nevertheless, of 24 patients who complained of shortness of breath on mild to moderate exertion, all showed some improvement in effort tolerance after operation. No doubt in some instances this was partly psychogenic, but respiratory function studies indicated improvement, ranging from moderate to striking, in all except 2 of the 25 cases investigated. In the early period after decortication pulmonary angiograms demonstrated a poor flow through the branches of the pulmonary artery; later this flow improved with corresponding increase in oxygen uptake. Patton et al.,[3] who studied lung function in a series of patients up to three years after decortication, also found steady improvement; the final result was not closely related to the duration of the condition before operation, but where parenchymal disease is extensive, little improvement in function can be expected.

Where the extent of parenchymal disease is slight and the remainder of the lung is healthy, Savage and Fleming confidently expect a good result, provided due attention is paid to management. Preoperatively chemotherapy and physiotherapy are important, and great care is necessary during the operation to avoid damaging the thoracic duct and the vagus and phrenic nerves. Mistakes in postoperative management can nullify the best efforts of the surgeon, and it is in this respect that the Sully contribution is chiefly helpful. Savage and Fleming suggest that, if disease is not widely scattered through the lung, its failure to expand after decortication is due to inability to deal with the air-leaks and the fluid which collects in the pleural space in the early postoperative days. The lung should be fully expanded at the earliest possible moment and kept so until all air-leaks have ceased. Continuous suction is applied to the drainage tubes through water-seal bottles as soon as the patient returns to the ward, and the tubes are not removed till they have ceased functioning. The patient is nursed on the unoperated side, and on the second or third day is put into a special hyperextension plaster which has been made for him preoperatively; in this position the mediastinum tends to fall to the opposite side, the diaphragm is carried caudally, and the ribs are stretched apart—the reverse of the situation before operation. The patient continues to lie in the plaster-cast, except for meals, for three to six weeks until chest expansion is equal on both sides or has reached its maximum, thereafter it is used for sleeping until three to six months have elapsed. Breathing exercises are begun on the first postoperative day and are continued for six months; all postoperative care is guided by frequent radiographs taken, with portable apparatus, at least twelve-hourly in the early stages.

There were no deaths in the series, and the few complications were not serious; tension pneumothorax and extensive surgical emphysema were not met with, having been prevented by multiple drainage tubes with suction. The results, indeed, are encouraging enough for Savage and Fleming to state: "There is no doubt that functional improvement of significant degree can be achieved in most cases, and we are prepared to recommend operation on that ground alone." Postoperative care is the keynote to success. The management of thoracic surgical patients demands a high level of training and team work, which nowadays, owing to shortage of skilled personnel, is not easily maintained. Attention to this vital factor is urgently required at many chest hospitals if they are to continue to meet their obligations as competently as they would like.

1. *Lancet*, 1954, i, 34.
2. Savage, T., Fleming, H. A. *Thorax*, 1955, **10**, 293.
3. Patton, W. E., Watson, T. R., Gaensler, E. A. *Surg. Gynec. Obstet.* 1952, **95**, 477.

DIURESIS AND DIURETICS

AT the Royal Society of Medicine on Feb. 28, Dr. D.A.K. Black defined the fundamental differences between water diuresis, in which solute excretion is slightly if at all increased, and osmotic diuresis, in which urinary solute is always increased. In diuretic therapy it is essential to enhance the output of sodium, and therefore all effective diuretics must cause osmotic diuresis. Diuretics can be used with advantage in states where oliguria and œdema are combined. Dr. T. Hanley said that he has found acetazolamide ('Diamox') inferior to mercurials; its efficacy diminishes with continued use, owing to reduction of plasma-bicarbonate and acidosis. Dr. M. D. Milne agreed with this view, and reviewed means of augmenting the effectiveness of mercurial diuretics. He recommended measures to increase plasma-chloride (e.g., ammonium and potassium chloride by mouth, ion-exchange resins in the ammonium cycle, or acetazolamide itself) and to increase the glomerular filtration-rate (e.g., intravenous aminophylline given about two to three hours after injection of the mercurial). Cases have recently been reported in which a nephrotic syndrome has developed during prolonged therapy with mercurials. It is difficult to be certain that the renal damage is actually due to mercurial toxicity, but therapy should certainly be discontinued if proteinuria steadily increases.

CANCER AND THE PUBLIC

INSTRUCTION of the public about cancer has no stronger advocate or exponent than Mr. Malcolm Donaldson, who believes that suitable explanation allays more apprehension than it causes[1] and is likely to bring patients to their doctor at an earlier and more curable stage of their disease. The effect of "cancer education" on the time of diagnosis of "accessible" cancers—i.e., those usually causing symptoms fairly early in their course—is examined in his report on a survey he made in 1954-55 on behalf of the Yorkshire Council of the British Empire Cancer Campaign.[2]

In an area comprising York, Hull, and the East Riding, with a population of about 600,000, 210 lectures on cancer were given to the lay public during two years. At the end of most of these lectures ballot-papers were distributed asking the audiences whether the lectures had relieved their anxiety or increased it, and whether they thought more should be given. Of more than 6000 votes 99% were in favour and only 0.2% against. In addition, more than 50,000 pamphlets were distributed; articles were published in the press; posters advertising the campaign were displayed; and diagrams explaining cancer and its treatment were shown in local health exhibitions. Nurses, health visitors, and midwives were given special lectures to enable them to discuss cancer with patients. The value of these measures appeared most convincing in cancer of the rectum, where the proportion of patients reporting symptoms with less than a month's delay rose from 16.9% to 33.7% and 43.8% during successive six-monthly periods. There was a slight rise in the equivalent figures for cancer of the breast, which were 35%, 37.7%, and 39%; but those for the uterus showed no material improvement—partly because patients found it hard to distinguish physiological from pathological bleeding. There were so few cases of cancer of the larynx, mouth, tongue, and bladder that the results were inconclusive, and in cancers of the skin early diagnosis is relatively unimportant.

As Donaldson says, this Yorkshire experiment, and the Manchester survey[3], "should prove to be of real value to any other local health authorities who are proposing to carry out cancer education of the public, which is so stongly advocated by the Ministry of Health." The results of the two pilot

1. *Lancet*, 1955, i, 959.
2. Report of Pilot Experiment in Cancer Education of the Public. By Malcolm Donaldson, F.R.C.S., F.R.C.O.G. Obtainable from the author at 337, Woodstock Road, Oxford. Pp. 34. 5s.
3. Paterson, R., Aitken-Swan, J. *Lancet*, 1954, ii, 857.

experiments justify, in his view, a far larger investigation in an area with a population of at least a million and lasting five to ten years so that patients may be adequately followed up.

NON-EXPLOSIVE ANÆSTHETICS

It seems that the risk of an explosion during an operation is of the order of 1 in 485,870.[1] This very occasional hazard can be eliminated only by the routine use of non-explosive anæsthetic agents. There are many such drugs, but usually several must be administered in combination.

In 1951 Cullen and Gross[2] reported that the non-explosive gas, xenon, was an efficient anæsthetic agent in man, being a little more potent than nitrous oxide. Cullen et al.[3] have shown that it produces only very slight biochemical and physiological disturbances during clinical anæsthesia maintained for as long as 2 hours 21 minutes. Now Bracken et al.[4] have confirmed experimentally the safety of brief administration of xenon and have designed an apparatus for investigating the long-term effects of this and other rare gases. No toxic effects were found macroscopically or microscopically in a rabbit which breathed xenon for 48 hours.

Xenon is extremely expensive and is not potent enough to be of practical value as an anæsthetic; but pilot investigations of this sort are important, since there is a definite need for an all-purpose, non-explosive inhalational anæsthetic.

HEROIN

The case against banning heroin was presented fully to the Society for the Study of Addiction on Feb. 21. Mr. Lawrence Abel said that in treating cancer one needs as many drugs as possible so as to ring the changes. 10–15% of people cannot tolerate morphine, and when a patient needs heroin he does need it. Morphine can cause spasm of the bile-ducts so that pressure is built up, and he thought the high incidence of trouble after cholecystectomy in the United States may be due to using morphine instead of heroin. Dr. A. H. Douthwaite said that, unlike morphine, heroin does not cloud the mind and allows people to attend to their affairs: to find a drug which relieves pain, produces euphoria, and does not impair the intellect, yet does not produce addiction, would be impossible. Because morphine so often induces vomiting, he has forbidden its use in his wards in cases of gastric hæmorrhage. Dr. Reginald Hale-White pointed out that in incurable disease euphoria may be as valuable as freedom from physical pain: when heroin is given the whole household cheers up. Dr. J. A. Hobson believed that if heroin ceases to be obtainable from medical sources the price will rise to a level at which professional drug pedlars will be attracted; they will smuggle in more of the drug and it will be worth their while to produce more addicts. Prof. A. D. Macdonald concluded that as analgesics, none of the substitutes are quite in the same class as heroin, and there is no really well-established case for suppressing it.

Two of the advertised speakers being absent, Prof. P. O. Wolff, formerly of the World Health Organisation, was left almost unaided to state the case in favour of the ban[5]. In answer to questions he explained that by its constitution W. H. O., as an essentially medical body, has no responsibility for controlling the illicit drug traffic, and is concerned simply with drug addiction arising from medical practice. Even the United Nations cannot impose a ban: they can do no more than ask governments to coöperate. Dr. Wolff believes that doctors must be free to prescribe what they think necessary, and he said that governments which have banned heroin (including that of the U.S.A.) do in fact keep small supplies which are obtainable by doctors who think the drug indispensable for a particular patient. He believes too that a government should not impose a ban without the agreement of the medical profession. But he pointed to the example of Switzerland, which in 1931 declared heroin indispensable, yet twenty years later abolished its use – not because Switzerland had an addiction problem of her own but because Swiss doctors no longer found heroin a necessity and the government wished to coöperate with other countries in suppressing the drug, in order to "fulfil a humanitarian task which is in keeping with its traditions". Apart from the United Kingdom, only four countries out of some eighty members of W. H. O. have not declared their willingness to dispense with heroin, and Professor Wolff hoped that on further consideration the profession in this country too will find heroin "ripe for replacement". Among the substitutes for it he drew attention particularly to the usefulness of dextromethorphan for cough and of levorphan for pain, which he thought worth further trial here.

Mr. Abel seemed to resent any suggestion that British doctors may be less than fully informed on anything that might benefit their patients; but Sir Weldon Dalrymple-Champneys felt that they have at any rate shown regrettably little interest in the treatment of intractable pain with cobra venom, which in some cases gives remarkable relief. Dr. Jeffrey Bishop regarded the proposed international ban on heroin as an attempt to bolster up the policy of the head of the (non-medical) American Narcotics Bureau—a policy which he said was increasingly discredited at home. To which Professor Wolff replied (1) that each delegation at the Commision of Narcotic Drugs of the Economic and Social Council of the United Nations acts on the instructions of its own government, and (2) that the American Medical Association, a body which certainly does not take orders from the Narcotics Bureau, has not opposed the Congressional prohibition of heroin in medical practice.

1. Report of the Ministry of Health, 1954. Part II; p. 168. H.M. Stationery Office, 1955.
2. Cullen, S. C. Gross, E. G. *Science*, 1951, **113**, 580.
3. Pittinger, C. B., Moyers, J., Cullen, S. C., Featherstone, R. M., Gross, E. G. *Anesthesiology*, 1953, **14**, 10.
4. Bracken, A., Burns, T.H.S., Newland, D.S. *Anaesthesia*, 1956, **11**, 40.
5. We hope later to publish extracts from his paper.

Letters to the Editor

Poliomyelitis Vaccination.—Dr. Goffe, in his letter last week, estimates the chance of young children contracting paralytic poliomyelitis as 1 in 3000 per year, and hopes that the British Salk-type vaccine will reduce this to 1 in 12,000 per year. In order to prevent 3 paralytic cases 12,000 children must each be given two or more injections of inactivated virus. This might be worth while if the protection lasted, but unfortunately it may only persist for a year or two. What will be the situation after five years as regards the millions of American children who have been given the inactivated virus? Will the partial protection be maintained, lost, or even reversed? It seems to many that the long-term prospects for those now being given the Salk-type vaccine are so uncertain that the present American programme may be correctly described as a gigantic gamble.—W. RITCHIE RUSSELL, F.R.C.P. (Oxford).

Barbiturate Poisoning.—Your leading article (Feb. 18) encourages me to draw attention to Gould's work in the treatment of this condition. His article quoted in your leader was the first of a series in which the clinical scope and physiological rationale of the treatment of acute barbiturate intoxication and allied conditions were discussed (J. Gould, *Lancet*, 1953, i, 590; *Brit. J. Addict.*, 1954, No. 1; *Proc. R. Soc. Med.* 1954, **47**, 215. R.W. Armstrong, J. Gould, *J. ment. Sci.* 1955, **101**, 70. J. Gould. B. S. Cooper, *Med. Pr.* 1955, **234**, 138). Gould maintains that intracellular brain katabolism is impeded in these states; and the later work of R. A. Hunter et al. on vitamin B_1 (*Lancet*, 1955, ii, 1353) supports his clinical deductions. Novelli and Soodak suggest that, for the reconstitution of dissociated enzyme and co-enzyme systems, up to 1000 times the normal tissue concentrations of co-enzyme—usually a B vitamin—may be required (Biochemistry and Physiology of Nutrition; vol. 2, p. 328). This is in close conformity with Gould's clinical observations and practice.

Physicians unfamiliar with these ideas are necessarily puzzled by the enormous doses of vitamins recommended by Gould and his co-workers in my department; but the high dosages are clinically demanded and would appear to be scientifically justified by the work of Novelli et al. In other words, in the treatment of barbiturate intoxication by high-potency vitamins we are no longer thinking of these in terms of normal nutritional needs, but are using them as powerful biochemical agents.

Another feature of the technique which has bothered critics is the continued administration of large amounts of balanced vitamins after the initial injection. The reason for this becomes clear when it is remembered that the gut and tissue-fluids remain for a very long time reservoirs of absorbable barbiturate which can only be exhausted by gradual absorption into the blood-stream.

"Conservative" methods of treatment were advocated by S. Locket and J. Angus (*Lancet*, 1952, i, 580); but it is surely desirable on physiological grounds to reduce the time during which brain-cells are subjected to biochemical insult.

We do not claim that the use of high-potency vitamins provides the whole—or even the most effective—method of treatment, but we do suggest that the striking clinical results which we have observed can be accounted for in terms of known enzyme chemistry.

The interest shown by clinical psychiatrists in this field should not come as a matter of surprise, in view not only of the rapidly increasing use of barbiturates in attemped suicide but also of the interesting psychiatric syndromes resulting from the use of barbiturates as sedative drugs during the day and hypnotics at night over long periods. In my department these syndromes—often unrecognised—have come to be known unofficialy as "chronic subclinical barbiturate intoxication."

These considerations make the continued collaboration of clinicians and biochemists a matter of urgency to meet what may without exaggeration be regarded as a social menace.—E. B. STRAUSS, F.R.C.P. (St. Bartholomew's Hospital, London, E.C.1.)

Tuberculosis and Liver biopsy.—Dr. Engstedt suggests (Feb. 25) bone-marrow aspiration in cases of tuberculosis. In 1952 Mr. Barton and I reported on examination of rib bone-marrow in patients undergoing surgical treatment (*Lancet*, 1952, ii, 1059). We were unable to demonstrate tubercle bacilli either by smear or culture. We suggested that the ribs removed in thoracic operations could be used in orthopædic units for grafting. But subsequently Dr. Lack pointed out that he knew of two cases of tuberculosis which had occurred when ribs from tuberculous patients had been used for spinal fusion for scoliosis (*Lancet*, 1952, ii, 1182). He suggested that if the aspirated bone-marrow had been placed in a muscle pouch of the guineapig, our results might have been different; but we have had no opportunity to carry out this work.—KENNETH MARSH, D.M. (Chest Clinic, Camberwell, London, S.E.5.)

The Future of the Chest Service.—Dr Macdonald (Feb. 25) has pointed the right way for the future.

Despite the moans about "splitting" of the old tuberculosis service, the chest services have have been one of the successes of the National Health Service. Thanks to improved diagnostic and therapeutic facilities, pulmonary tuberculosis is being brought under control. It is, however, far too little recognised that many clinics and sanatoria have been doing increasing amounts of non-tuberculosis chest work and penetrating an unexplored field of chronic invalidism. Much of this invalidism is preventable, and, as Dr. Macdonald says, the sociomedical problems of, say, chronic bronchitis are strikingly similar to those of the patient with tuberculosis.

The chest services, with their staffs of physicians, health visitors, and almoners, and using the welfare facilities of the local authorities through the medical officers of health, are in an exellent position to launch an all-out attack on chronic respiratory disease. The indications are for expansion, not contraction, and for progressive integration with the general-hospital services. Initial expenditure would not be high and dividends would very soon come in.—GWYN HOWELLS, M.R.C.P. (Littleover, Derby.)

Gluten to Blame?—Your annotation (Feb. 25) suggests that at the Royal Society of Medicine I attributed the "precœliac syndrome" to agene. In fact I was as careful to avoid such a specific imputation as I was in my letter of Feb. 18. Observations on my cases suggest that the "staling" process of flour may be connected with the cause of this syndrome. Flour may become stale through being kept too long, or it may attain similar properties as the result of treatment by the various "improving" processes to which it is usually subjected.

In the past three years at a residential nursery-school here I have seen no case of the precœliac syndrome, notwithstanding a number of epidemics including measles. The reason may be that the bread, biscuits, and cakes included in the children's diet are made only from fresh untreated stone-ground flour.

Recent research has shown that when flour becomes stale there is a progressive loss of its vitamin-E content, and this vitamin is quickly and completely destroyed when the flour is treated by agene or chlorine dioxide. This might suggest that a vitamin-E antimetabolite plays a part in the ætiology of the precœliac syndrome.

The patient-to-patient variation in the manifestations of cœliac disease was brought forward as an argument against the connection between this disease and the syndrome I have described. There is considerable variation from patient-to-patient also in the precœliac syndrome when symptons have been present for two months or more; it is only in the early weeks that the signs are so consistent.

Your annotation suggests that there is little resemblance between canine hysteria and cœliac disease. Veterinary workers recognise that canine hysteria can occur when a dog eats no agenised bread; thus methionine sulphoximine is not the only cause of this condition in dogs, and I have never suggested that it was the only cause of the precœliac syndrome. Canine hysteria due to causes other than agene, after having been present for a few months, resembles cœliac disease quite closely, apart from the fits. The dogs lose weight, have distended abdomens, have poor appetites, are bad-tempered and unfriendly, and may have pale, bulky, foul-smelling stools. Also as in cœliac disease, these symptoms are greatly aggravated by infections.

Clearly much further research is needed to elucidate the cause of this syndrome; whatever this may prove to be, at least we have in the gluten-free diet a valuable symptomatic treatment to speed convalescence after infections, which will be appreciated by both patients and parents.—GUY DAYNES, M.R.C.S. (Hove, Sussex.)

Production of Codeine—I agree with Dr. Williams (Jan. 21) that the amount of codeine in tab. codein. co. does not enhance the analgesic value. It does, however, produce side-effects, in particular constipation, which limits its continued use in such common conditions as the chronic rheumatic diseases.

Recently I have compared the effect of a new analgesic, *n*-acetyl-*p*-aminophenol ('Panadol,' Bayer Products) with tab. codein. co. in 20 cases of chronic rheumatic disease found in my general practice. Side-effects developed in 12 cases on tab. codein. co., but in only 1 on panadol. It appears that this new drug has an analgesic value equal to that of tab. codein. co. with the advantage of having fewer side-effects.

In my opinion the only effect of stopping the production of codeine would be, as Dr. Williams implies, to reduce the consumption of laxatives.—R. R. HAMILTON. M.B. (Hawick Roxburghshire.)

Prevention of Hay-fever.—At this time of year, when hay-fever sufferers are beginning some form of prophylactic treatment, my experience with a patient who has had hay-fever for over thirty years may be of interest.

Using 'Pollacine' vaccine (Parke, Davis), in fourteen doses I have advanced from 500 units to 30,000 units by administering, as an adjunct to the vaccine, chlorpromazine maleate ('Piriton Maleate', Allen & Hanburys) 10 mg. in 1 ml. This is added to the recommended dose of pollacine with a small amount of lignocaine to reduce the absorption and the pain from a 2 ml. injection into the deltoid muscle. The patient has had no untoward reaction. He carries with him as a safety measure tablets of piriton, with instructions to take two (8 mg.) at once if there is any delayed reaction. To date this has not been necessary. He is inclined to be drowsy by early afternoon, and this is overcome by his taking one tablet of 'Preludin' (Pfizer) during the morning. At this rate the total course of some sixty injections, ranging from 500 to 150,000 units, can be reduced by two-thirds, with a substantial saving of both doctor's and patient's time.

The advantage of piriton over other anti-histamine substances which have been administered to this patient is the very slight reaction.—DOUGLAS STATHERS, M.R.C.S. (Caterham, Surrey.)

New Kidneys for Old.—I agree with your views as to the possible importance of kidney transplantation as an eventual therapeutic goal. It would seem unfortunate, however, that you apparently remain ignorant of the work in this field carried out in this country. May I draw attention to some of the errors in your leading article of Feb. 18:

(1) The problem of renal homotransplantation was not discussed at the Ciba symposim in 1954 (Preservation and Transplantation of normal tissues. London, 1954).

(2) Your reference for the evidence of common antigenicity of skin and kidney cites a paper (R. E. Billingham et al. *Ann. N. Y. Acad. Sci.* 1955, **59**, 409) which does not consider this problem let alone give any evidence. The two relevant publications are as follows: M. Simonsen, F. Sorensen, *Acta chir. scand.* 1949, **99**, 61. W. J. Dempster, *Brit. J. plast. Surg.* 1953, **5**, 228.

(3) Your reference to a paper by us (W. J. Dempster, A. M. Joekes, *Quart. J. exp. Physiol.* 1953, **38**, 11) as showing that transplanted kidneys with the ureters implanted "into organs other than the bladder" deteriorate rapidly in function is inept. This paper dealt exclusively with some problems of diuresis and antidiuresis in autotransplanted kidneys with skin ureterostomy.

Work in this country has had as one of its major aims to confirm technical feasibility of transplanting kidneys, known since the turn of the century, and to establish the best site for long-term survival and maintenance of function (W. J. Dempster, A. M. Joekes, *Acta med. scand.* 1953, **147**, 99. W. J. Dempster, A. M. Joekes, N. Oeconomos, *Ann. R. Coll. Surg. Engl.* 1955, **16**, 324). Reimplantation of the ureter into the bladder resulted in better function of transplanted kidneys, which showed indefinite survival-times with normal function.

It is surprising that you follow the paper from Boston (J. P. Merrill et al. *J. Amer. med. Ass.* 1956, **160**, 277), describing the successful homotransplantation of a kidney between identical twins, in failing to cite the only published work, done in this country, giving clear indications for the elective site for a kidney transplant.—A. M. JOEKES, M.R.C.P. (London, W.1.)

Obituary

Miss DIANA BECK

Miss Beck, neurosurgeon to Middlesex Hospital, where she died on March 3, was one of the first women to be appointed to the consultant staff of a London teaching hospital which was not her own. Born in 1902 in Chester, of a family of Scottish descent, she qualified from the Royal Free Hospital, London, in 1925. Having taken the F.R.C.S. in 1930, she returned to the Royal Free as surgical registrar and lecturer in surgical anatomy, and she had already proved herself as a surgeon and teacher before she specialised in neurosurgery. Shortly before the late war she began her apprenticeship in this exacting specialty with Hugh Cairns at Oxford. In 1943 she was appointed neurosurgeon to the Royal Free Hospital. She worked at Chase Farm and in Bristol where she had charge of an E.M.S. neurosurgical unit. She joined the staff of Middlesex Hospital in 1947

Prof. L. P. GAMGEE

THE Gamgee family belong to the history of Birmingham surgery, and Professor Gamgee, who died on March 1 at the age of 87, belonged to the second generation. His father, Sampson Gamgee, who joined the staff of the Queen's Hospital almost a century ago, will be remembered for his advocacy of dry infrequent dressing of wounds and also his promotion of the Hospital Saturday Fund. Leonard Gamgee qualified in 1891 from Queen's College, Birmingham, and his first appointments were as assistant to the professor of surgery and as a resident at the Queen's Hospital. He joined the staff of the Birmingham General Hospital in 1893 and later was appointed to the chair of surgery in the university. His teaching was practical and effective. He had the knack of setting out surgical principles clearly and entertainingly, and the courage to set them out dogmatically, for he was unwilling to confuse his students with differing opinions and authorities. As a colleague put it, his students were told "what to do and when to do it and as often as not made to do it there and then". Gamgee belonged to the age of clinical rather than laboratory surgery and he was content to write little and practise much, treating patients rather than diseases.

In England Now

O what can ail *The Lancet's* form,
Alone and palely loitering?
The ink is wither'd from the page,
And no printers print.

News

Influenza-like illnesses have been increasingly common in the past few weeks in many parts of the country. In the north, Cumberland, Lancashire, and Cheshire have been particularly affected. Elsewhere, the outer London area, especially Kent and Sussex, has been among the many areas involved. Virus A has again been demonstrated in many outbreaks.

On Feb. 25 at a congregation of the University of Oxford the degree of D.M. was conferred on A. W. Frankland, Margaret E. H. Turner Warwick, and H. A. K. Rowland, and the degree of B.M. on Joyce Dutton.

At recent examinations for the degree of M.CHIR. in the University of Cambridge the following were successful: D. A. Bailey, J. M. Davis, C. Q. Henriques, P. F. Jones, D. W. T. Roberts, T. M. Robinson, W. F. W. Southwood.

The University of Dublin is to confer the honorary degree of M.D. on Dr. E. R. Boland and the honorary degree of M.CH. on Prof. A. K. Henry.

At recent examinations of the Royal Colleges of Physicians and Surgeons of Edinburgh and the Royal Faculty of Physicians and Surgeons of Glasgow for the diploma of L.R.C.P.E., L.R.C.S.E., L.R.F.P. & S., the following were successful: S. J. Benjamin, D. A. Blair, K. M. Cohen, W. D. Dodds, Noorali Devji Dhanji, William Irvine, Wah Lean Low, Alan McEwan, A. H. Macgregor, Cheng Hooi Ong, J. J. Robb, Chun Yuen Su.

The late Dr. Ethel Townend, of Hull, has left about £50,000 on trust for "necessitous members of the medical and other professions".

Mr. John Anderson, deputy secretary of the Scottish Home Department, has been appointed secretary of the Department of Health for Scotland.

The fellowship of University College, London, has been conferred on Prof. D. V. Davies, St. Thomas's Hospital.

The council of St. Mary's Hospital Medical School gave a dinner on Feb. 29 in honour of Mr. Edgar E. Lawley, chairman of the medical school centenary fund council. Mr. Lawley said the fund now amounted to £185,000, and there were good hopes that it would eventually reach £200,000.

The annual general meeting of the Haemophilia Society will be held on March 18 at 3.30 P.M. at St. Pancras Town Hall, London, N.W.1. The president, Sir Lionel Whitby, will give an address.

Dr. E. J. C. Hewitt has been appointed a medical commissioner of the General Board of Control for Scotland.

International scholarships in anæsthesiology for woman doctors have been established at the New England Hospital, Boston, Massachusetts. Candidates from English-speaking countries are eligible for a scholarship which includes a stipend of $1800 a year, full maintenance, and travelling expenses.

Appointments

DOHERTY, J. K., L.R.C.P.I., D.P.H.: asst. M.O.H. and school M.O., Oldham.

EARLE, J. H. O., M.D. Lond.: clinical pathologist, Royal Masonic Hospital, London.

FISCHER, EMANUEL, PH.D. Prague, L.R.C.P.I., D.P.M.: consultant psychiatrist and deputy medical superintendent, Little Plumstead mental-deficiency group of hospitals.

HOPE, MARGARET, M.B. Edin., D.C.H.: asst. M.O., Dumfriesshire.

KELLOCK, W., F.R.C.S.: senior orthopædic registrar, United Norwich Hospitals.

LADELL, W. S. S., M.B. Camb.: research physiologist, Ministry of Supply.

MCELROY, R. S., M.B. Dubl., D.P.H., D.T.M.: M.O.H. and area M.O., Meriden and Tamworth R.D.s.

Vacancies

ACADEMIC AND EDUCATIONAL

Sheffield University. Lecturer in Med.

Sheffield University. Lecturer & Demonstrators in Anatomy.

Oxford University Asst. Graduate in Path.

University of London. Lecture "Some New Aspects of Action of Morphine-like Analgesics". 14th March.

Royal College of Surgeons of England. Annual Examinerships.

Royal College of Surgeons of England. Election of Professors and Lecturers.

Royal College of Surgeons of England. Sir William Lister Award in Ophthalmology (Travelling Scholarship).

Middlesex Hosp. Med. School. Prize in Applied Pharmacology.

British Psycho-Analytical Society. Freud Centenary Lectures.

Glasgow University. Lectureship in Medicine.

Johannesburg, S. Africa. University Witwatersrand. (Pathology Dept.) 2 Full-time Chairs.

Nuffield Foundation, N.W.1. Travelling F'ships. in Med.

Sheffield University. Course of Instruction (D.P.H.). 1st Oct.

Chester Beatty Research Inst. Royal Cancer Hosp., S.W.3. Sr. Tech.

Liverpool University. (Biochem. Dept.) Asst./Lecturers or Lecturers.

Leeds University. I.C.I. Research F'ships.

ANÆSTHETICS
King Edward Mem., W. Sr. H.O.
Prince of Wales's Gen., N.15. Sr. H.O.
Barrow & Furness H.M.C. Jr. H.M.O.
Birmingham. Dudley Road. Sr. H.O.
Ethiopia. Princess Tsahai Mem. Addis Ababa. Anæs.
Kettering & Dist. H.M.C. Sr. H.O.
Manchester R.H.B. & United Hosps. P.-t Cons.
Northampton Gen. H.O.
Oxford United Hosps. Sr. H.O.
Stafford H.M.C. Sr. H.O.
U.S.A. Cambridge, Mass. Residencies
Welsh R.H.B. Cons.

CASUALTY
Hackney, E. 9. H.O.
Lambeth, S.E.11 Sr. H.O. or H.O.
West London, W.6. Sr. H.O.
Brighton. Royal Sussex County. H.O.'s.
Canterbury. Kent & Canterbury. Sr. H.O.
Cardiff. St. David's. Sr. H.O.
Cheltenham Gen. & Eye. Sr. H.O.
Chesterfield Royal. H.O.
Dudley, Stourbridge & Dist. Sr. H.O.
Northampton Gen. Sr. H.O. & H.O.
Reading. Battle. H.O.
Weston-super-Mare Gen. Sr. H.O.

CHEST AND TUBERCULOSIS
North West Met. R.H.B. Reg.
Birmingham R.H.B. Reg.
Cardiff. Glan Ely. Sr. H.O.
Chelmsford. Broomfield. Locum Sr. H.M.O.
Driffield. Northfield San. Sr. H.O.
Ipswich. St. Helen's. H.O.
Manchester R.H.B. Reg.
Scotland. Eastern R.H.B. Reg

DERMATOLOGY
Royal Free Hosp. Group. P.-t. Cons.
Glasgow. Stobhill Gen. Pre-reg. H.O.

EAR, NOSE, AND THROAT
Hosp. for Sick Child. W.C.1. Reg.
Metropolitan E. N. & T., W.8. H.O.
Royal National T. N. & E. & Inst of Laryngology & Otology. Sr. Reg.
Blackpool. Victoria. Sr. H.O.
Doncaster Royal Infy. Sr. H.O.
Hull. Victoria Hosp. for Sick Child. Locum Sr. H.O.
Northampton Gen. Sr. H.O.
Portsmouth Group H.M.C. Sr. H.O.
Reading. Royal Berks. H.O.
Southampton. Royal South Hants. & Gen. Sr. H.O.

GERIATRICS
East Anglian R.H.B. Sr. H.M.O.
Glasgow. Stobhill Gen. Pre-reg. H.O.

INFECTIOUS DISEASES
Portslade. Foredown. Jr. H.M.O.

MEDICINE
Bethnal Green, E.2. H.O.
Fulham, W.6. Reg.
Queen Mary's Hosp. for East End, E.15. H.O.
South Lodge, N.21. H.O.
St. Leonard's, N.1. Sr. H.O.
Birmingham. Dudley Road. H.O.
Birmingham R.H.B. P.-t. Cons.
Birmingham R.H.B. Reg.
Bournemouth. Christchurch. Reg.
Bournemouth. Royal Victoria. H.O.
East Anglian R.H.B. Reg.
Enfield. Chase Farm. Sr. H.O.
Enfield. War Mem. Sr. H.O.
Glasgow Royal Infy. Sr. H.O.
Huntingdon County. H.O.
Ilford. King George. Pre-reg. H.O.
Ipswich & East Suffolk. Sr. H.O.
Luton & Dunstable. Reg.
Maidenhead. H.O.
Manchester R.H.B. Reg.
Portsmouth Group H.M.C. Sr. H.O.
Scunthorpe. War Mem. Pre-reg. H.O. or Sr. H.O.
Stoke-on-Trent. City Gen. H.O.
Swansea. Mount Pleasant. Jr. H.M.O.
Torquay. Torbay. Sr. H.O.
Tredegar, Mon. St. James. H.O.

NEUROLOGY
National Hosp. for Nervous Diseases. Reg.
South West Met. R.H.B. Cons.

OBSTETRICS AND GYNÆCOLOGY
Hackney, E.9. H.O.
South London Hosp. for Women, S.W.4. H.O.'s.
St. Bartholomew's, E.C.1. Reg.
Birmingham. Marston Green Maty. H.O.
Birmingham R.H.B. Regs.
Birmingham United Hosps. Reg. & H.O.'s.
Bromsgrove Gen. Pre-reg. H.O.
Canterbury, Kent & Canterbury. H.O.
Cheltenham Maternity. H.O.
Croydon Group H.M.C. Locum Cons.
Doncaster. Western. Reg.
Halifax Area Hosps. M.C. Sr. H.O.
Hastings. Buchanan. H.O.
Manchester. R.H.B. Reg.
Manchester United Hosps. Sr. H.O. & H.O.
Nottingham. Firs Maternity. Sr. H.O.
Portsmouth Group H.M.C. Pre-Reg. H.O.
Reading Combined Hosps. H.O.'s.
Rochford, Essex, Gen. H.O.
Romford. Oldchurch. Sr. H.O.
Sheffield R.H.B. Sr. Reg.
Swansea. Sr. H.O.

OPHTHALMOLOGY
Manchester United Hosps. Sr. H.M.O.
Newcastle-upon-Tyne H.M.C. Sr. H.O.
Oxford United Hosps. H.O.

ORTHOPÆDICS
Royal National Orthopædic, W.1. Sr. H.O.
South-East Met. R.H.B. P.-t. Cons.
Alton. Lord Mayor Treloar Orthopædic. Locum Reg.
Bebington. Clatterbridge. Locum Jr. H.M.O.
Birmingham R.H.B. Reg.
Braintree. Black Notley. H.O.
Bridge of Earn, Perthshire. Sr. H.O. & H.O.
Brighton Gen. H.O.
Durham. County. H.O.
Isleworth. West Middlesex. Sr. H.O.
Medway & Gravesend H.M.C. Locum Reg.
Northampton Gen. H.O.
Oxford R.H.B. Reg.
Portsmouth Group H.M.C. Pre-reg H.O.
Romford. Oldchurch. H.O.
Southampton. Royal South Hants Sr. H.O.
Swansea. Sr. H.O.
Wigan. Royal Albert Edward Infy. Sr. H.O.

PÆDIATRICS
Hosp. for Sick Child., W.C.1. Sr. H.O.
St. James's, S.W.12. Sr. H.O.
Birmingham United Hosps. Sr. Reg.
Chelmsford. St. John's. H.O.
Luton & Dunstable. H.O.
Manchester. Duchess of York Hosp. for Babies. H.O.
Northampton Gen. H.O.
Reading. Royal Berks. H.O.
Canada. Child's. Hosp., Vancouver. Residents.

PATHOLOGY
Royal Marsden, S.W.3. Locum Sr. H.M.O. or Sr. Reg.
St. Bartholomew's. E.C.1. Sr. H.M.O.
Birmingham R.H.B. Regs.
Leeds R.H.B. Sr. H.M.O.
Macclesfield. Sr. H.O.
Manchester. West Manchester H.M.C. Sr. H.O.
Northwood, Middx. Mount Vernon. Sr. H.O.
Oxford R.H.B. Reg.
Oxford United Hosps. Locum Sr. H.O.
Rochford, Essex. Gen. Locum Reg. & Sr. H.O.
Sheffield United Hosps. Reg. or Sr. H.O.

PSYCHIATRY
Friern H.M.C., N.11. Jr. H.M.O.
Marlborough Day, N.W.8. P.-t. Reg.
North West Met. R.H.B. P.-t. Sr. H.M.O.
South-East Met. R.H.B. P.-t. Cons. & Sr. H.M.O.
St. George's, S.W.1. Reg.
Aylesbury. St. John's. Jr. H.M.O.
Birmingham R.H.B. Reg.
Brentwood. Warley. Sr. H.O
Exeter. Digby/Wonford. Jr. H.M.O.
Nottingham. Saxondale. Reg.
Oxford R.H.B Sr. H.M.O.
St. Alban's. Hill End. Reg.
Wallingford, Berks. Fair Mile. Jr. H.M.O
Wickford, Essex. Runwell. Sr. H.O.

RADIOLOGY
South West Met. R.H.B. P.-t Cons.
St. Bartholomew's, E.C.1. Sr. Reg.
Portsmouth Group H.M.C. Reg.
Sheffield R.H.B. P.-t. Cons.
Southend-on-Sea. Gen. Temp. P.-t. Cons. or Temp. Sr. H.M.O.
Watford & Dist. Peace Mem. Reg.
Welsh R.H.B. Locum Cons.
Welsh R.H.B. Cons.

SURGERY
Bethnal Green, E.2. H.O.
Hamersmmith Hosp. & Postgrad. Med. School, W.12. H.O.
Hosp. for Sick Child., W.C.1. P.-t. Sr. Reg.
Royal Marsden, S.W.3. H.O.
South-East Met. R H.B. P.-t. Cons.
South-East Met. R.H.B. Reg.
South Western, S.W.9. Sr. H.O.
St. George-in-the-East, E.1. H.O.
St. James's, S.W.12. Reg.
St. Leonard's, N.1. H.O.
Wanstead, E.11. H.O.
Barrow-in-Furness. North Lonsdale. H.O.
Batley, Yorks. Gen. Pre-reg. H.O.'s.
Blackburn & Dist. H.M.C. H.O.'s.
Birmingham Accident Hosp. & Rehab. Centre. Sr. H.O.'s.
Brighton. Royal Sussex County. H.O.'s.
Canterbury, Kent & Canterbury. H.O.
Carlisle. Cumberland Infy. H.O.'s
Carlisle. Cumberland Infy. Sr, H.O.
Carshalton, Queen Mary's Hosp. for Child. Reg.
Chelmsford & Essex. Locum Reg.
Chelmsford & Essex. Pre-reg. H.O.'s
Chesterfield Royal. H.O.
Derby, Derbyshire Royal Infy. Pre-reg. H.O. or Sr. H.O.
Doncaster Royal Infy. Sr. H.O.
Dudley, Stourbridge & Dist.. Sr. H.O.
Enfield. Chase Farm. H.O.
Halifax Gen. H.O.
Haslemere & Dist. H.O. or Locum.
Hastings. Royal East Sussex. Pre-reg. H.O.'s
Hastings. St. Helen's. Pre-reg. H.O.
Huddersfield Royal Infy. H.O.
Isleworth. South Middlesex. Pre-reg. H.O.
Leeds United Hosps. R.H.B. Sr. Reg.
Lincoln County. Pre-reg. H.O.
Liverpool. Mossley Hill. Jr. H.M.O.
Louth County Infy. Sr. H.O.
Maidenhead. Reg.
Manchester R.H.B.Reg.
Manchester. West Manchester H.M.C. Pre-reg. H.O.'s.
Manchester. Wythenshawe. Sr. H.O.
Northampton Gen. H.O.
Nottingham Gen. Pre-reg. H.O.
Nottingham Highbury. Sr. H.O.
Peterborough Mem. H.O.
Plymouth. S. Devon & E. Cornwall Gen. Pre-reg. H.O.
Porth & Dist. Jr. H.M.O.
Portsmouth Group H.M.C. Sr. H.O & Pre-reg H.O.
Preston Royal Infy. Reg.
Richmond, Surrey. Royal. Sr. H.O.
St. Alban's City. Locum Reg.
Stoke-on-Trent. City Gen. H.O.
Welsh R.H.B. Reg.
Welsh R.H.B. Cons.

THORACIC SURGERY
Ilkley. Middleton. Sr. H.O.

VENEREOLOGY
London, E.1. P.-t. Cons.

GENERAL
Oxford United Hosps. Sr. H.O.

PUBLIC APPOINTMENTS
National Coal Board. (South Western Div.) Asst. Area M.O.
National Coal Board. (North Eastern Div.) Area M.O.
Cheshire C.C. Asst. County M.O.
Ministry of Health H.Q. M.O.'s
Gold Coast Local Civil Service. Specialist Anæs.
British Guiana Govt. Lady Health Officer.
H.M. Oversea Service, Kenya. M.O.'s
Glasgow Corp. A.M.O. (Maty. & C.W.)
Staffordshire C.C. Asst. County M.O. & School M.O.
West Hartlepool County Borough. Deputy M.O.H. & Deputy Principal School M.O.

(Further particulars of above vacancies available on request to Advertisement Manager.)

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON & VINEY, LTD., London and Aylesbury—Saturday, March 10, 1956.
PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.